

sequence set forth in SEQ ID NO:113, and an L-CDR3 comprising the sequence set forth in SEQ ID NO:111, and

b) each antigen-binding polypeptide construct specifically binds an extracellular domain (ECD) of human epidermal growth factor receptor 2 (HER2); and

c) the first monovalent antigen-binding construct and the second monovalent antigen-binding construct bind to non-overlapping epitopes and do not compete with each other for binding to HER2; wherein constructs 1, 2, and 4 bind to ECD4 of HER2; and construct 3 binds to ECD2 of HER2; and construct 5 binds to an B1D2-binding ECD of HER2; and

d) each dimeric Fc is a heterodimeric Fc and each Fc polypeptide of each heterodimeric Fc is a human IgG1 Fc and comprises a distinct CH3 sequence, and one CH3 sequence comprises L351Y\_F405A\_Y407V and the other CH3 sequence comprises T366L\_K392M\_T394W; or

one CH3 sequence comprises L351Y\_F405A\_Y407V and the other CH3 sequence comprises T366L\_K392L\_T394W; or

one CH3 sequence comprises T350V\_L351Y\_F405A\_Y407V and the other CH3 sequence comprises T350V\_T366L\_K392L\_T394W; or

one CH3 sequence comprises T350V\_L351Y\_F405A\_Y407V and the other CH3 sequence comprises T350V\_T366L\_K392M\_T394W; or

one CH3 sequence comprises T350V\_L351Y\_S400E\_F405A\_Y407V and the other CH3 sequence comprises T350V\_T366L\_N390R\_K392M\_T394W, according to EU numbering.

**48.** The method of claim **47**, wherein treating the subject is inhibiting growth of the HER2+ tumor or delaying progression of the HER2+ tumor.

**49.** The method of claim **48**, wherein the HER2+ tumor is selected from a breast tumor, an ovarian tumor, a stomach tumor, a gastroesophageal junction tumor, an endometrial tumor, a salivary gland tumor, a head and neck tumor, a lung tumor, a brain tumor, a kidney tumor, a colon tumor, a colorectal tumor, a thyroid tumor, a pancreatic tumor, a prostate tumor, and a bladder tumor.

**50.** The method of claim **49**, wherein the HER2+ tumor is a breast tumor.

**51.** The method of claim **48**, wherein the first monovalent antigen-binding construct is construct 1 and the second monovalent antigen-binding construct is construct 3.

**52.** The method of claim **51**, wherein the heterodimeric Fc domain is coupled to the antigen-binding polypeptide construct with the linker, wherein the linker is a polypeptide linker, or comprises an IgG1 hinge region.

**53.** The method of claim **52**, wherein at least one of the first and second monovalent antigen-binding constructs of the combination is conjugated to a drug.

**54.** The method of claim **53**, wherein the drug is maytansine (DM1).

**55.** The method of claim **48**, comprising administering the combination of the first and second monovalent antigen-binding constructs in a pharmaceutical composition.

**56.** The method of claim **55**, further comprising administering an additional agent.

**57.** The method of claim **48**, wherein:

construct 1 comprises a heavy chain variable domain comprising the sequence set forth in SEQ ID NO:177 and a light chain variable domain comprising the sequence set forth in SEQ ID NO:243;

construct 2 comprises a heavy chain variable domain comprising the sequence set forth in SEQ ID NO:193 and a light chain variable domain comprising the sequence set forth in SEQ ID NO:243;

construct 3 comprises a heavy chain variable domain comprising the sequence set forth in SEQ ID NO:271 and a light chain variable domain comprising the sequence set forth in SEQ ID NO:87;

construct 4 comprises a heavy chain variable domain comprising the sequence set forth in SEQ ID NO:223 and a light chain variable domain comprising the sequence set forth in SEQ ID NO:215;

construct 5 comprises a heavy chain variable domain comprising the sequence set forth in SEQ ID NO:99 and a light chain variable domain comprising the sequence set forth in SEQ ID NO:107.

**58.** The method of claim **48**, wherein:

construct 1 comprises a first heavy chain comprising the sequence as set forth in SEQ ID NO:175, a light chain comprising the sequence as set forth in SEQ ID NO:241, and a second heavy chain having the sequence as set forth in SEQ ID NO:235;

construct 2 comprises a first heavy chain comprising the sequence as set forth in SEQ ID NO: 191, a light chain comprising the sequence as set forth in SEQ ID NO:241, and a second heavy chain having the sequence as set forth in SEQ ID NO:235;

construct 3 comprises a first heavy chain comprising the sequence as set forth in SEQ ID NO: 269, a light chain comprising the sequence as set forth in SEQ ID NO:85, and a second heavy chain having the sequence as set forth in SEQ ID NO:235;

construct 4 comprises a first polypeptide comprising the sequence as set forth in SEQ ID NO:213, and a second heavy chain having the sequence as set forth in SEQ ID NO:73;

construct 5 comprises a first polypeptide comprising the sequence as set forth in SEQ ID NO:97, and a second polypeptide having the sequence as set forth in SEQ ID NO:79.

**59.** The method of claim **57**, wherein the first monovalent antigen-binding construct is construct 1 and the second monovalent antigen-binding construct is construct 3.

**60.** The method of claim **58**, wherein the first monovalent antigen-binding construct is construct 1 and the second monovalent antigen-binding construct is construct 3.

**61.** The method of claim **47**, wherein at least one of the Fc polypeptides of the heterodimeric Fc comprises one or more modifications to promote selective binding of Fc-gamma receptors.

**62.** The method of claim **47**, wherein each of the Fc polypeptides of each heterodimeric Fc comprises CH2 sequence modifications L234A, L235A, and D265S.

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